

1/16

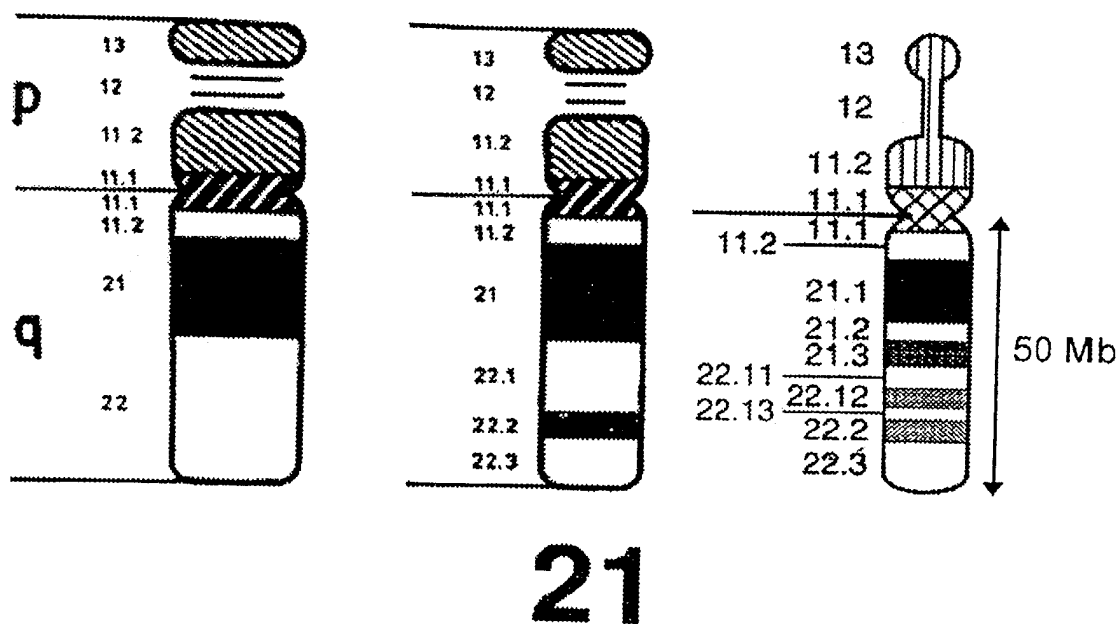


Figure 1

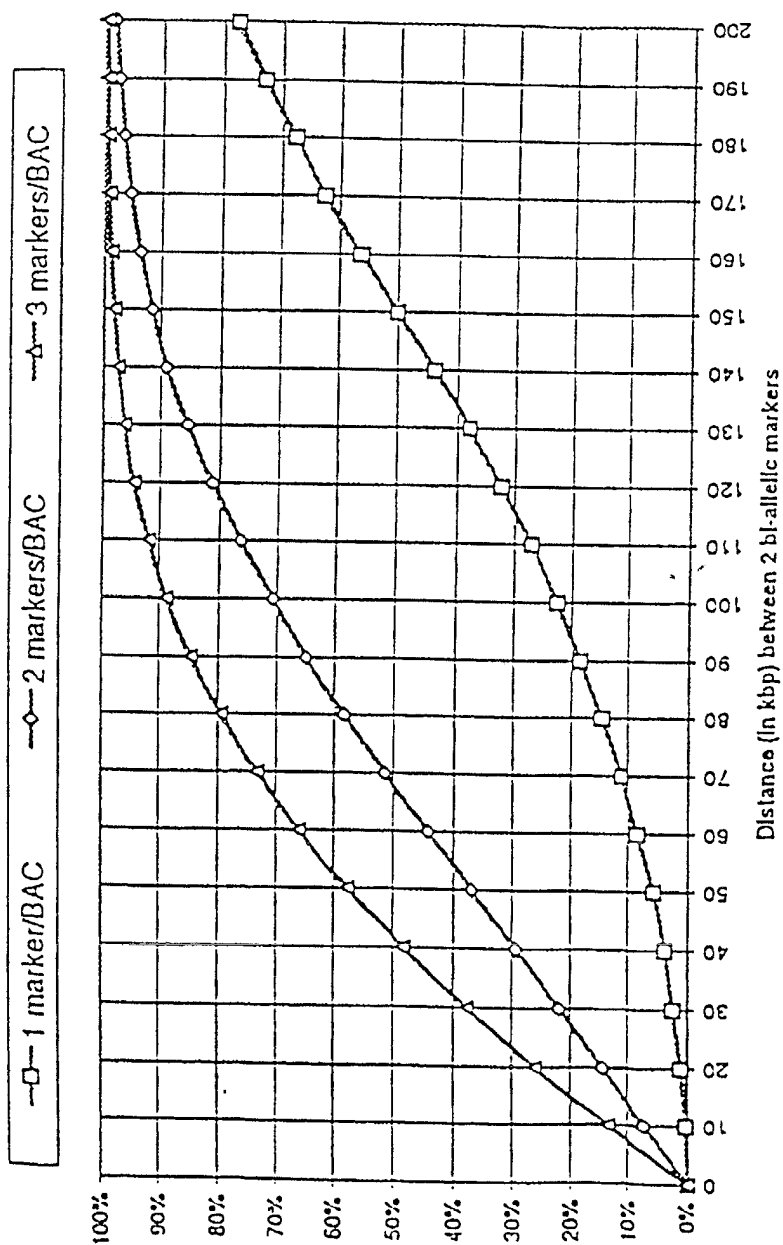


Figure 2A

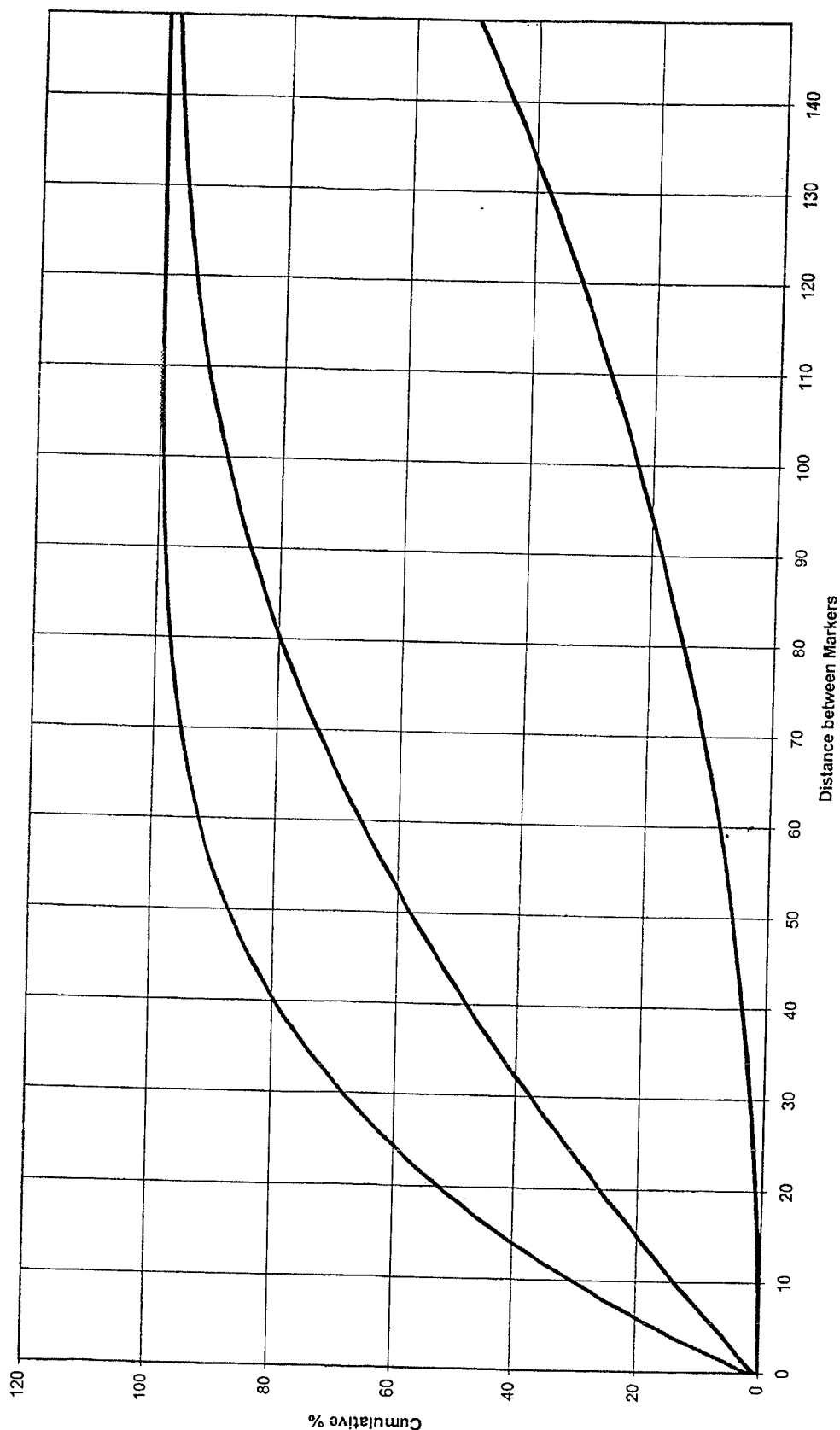


Figure 2B

p-VALUE DISTRIBUTION

# aff	150
# non aff	150
pAi	non aff
Δ pAi	0,05
Δ pAi	0,1
Δ pAi	0,15
Δ pAi	0,2
Δ pAi	0,25
Δ pAi	0,3
Δ pAi	0,35
Δ pAi	0,4
	0
	0,1
	0,2
	0,3
	0,4
	0,5

# aff	200
# non aff	200
pAi	non aff
Δ pAi	0,05
Δ pAi	0,1
Δ pAi	0,15
Δ pAi	0,2
Δ pAi	0,25
Δ pAi	0,3
Δ pAi	0,35
Δ pAi	0,4
	0
	0,1
	0,2
	0,3
	0,4
	0,5

aff affected individuals
 # non aff non affected individuals
 pAi non aff allele frequency in non affected individuals
 Δ pAi % Difference in allele frequency between affected and non-affected individuals

Figure 3 (I)

p-VALUE DISTRIBUTION

# aff	500								
# non aff	500								
pAi non aff		0	0,1	0,2	0,3	0,4	0,5		
Δ pAi	0,05	8,0004E-13	0,00072323	0,00741965	0,0169842	0,02371865	0,02516449		
Δ pAi	0,1	1,0695E-24	3,7948E-10	2,4176E-07	2,7579E-06	6,9679E-06	6,9679E-06		
Δ pAi	0,15	3,813E-37	1,0719E-18	5,8344E-14	4,2622E-12	1,8601E-11	1,1611E-11		
Δ pAi	0,2	2,9626E-50	5,0895E-29	1,6881E-22	6,9321E-20	3,7441E-19	6,9321E-20		
Δ pAi	0,25	4,2697E-64	7,2043E-41	7,7528E-33	1,194E-29	4,3462E-29	7,6438E-31		
Δ pAi	0,3	9,6976E-79	3,9328E-54	6,3017E-45	1,9429E-41	1,9429E-41	6,3017E-45		
Δ pAi	0,35	2,911E-94	8,8513E-69	8,7879E-59	2,3478E-55	1,8839E-56	1,1206E-62		
Δ pAi	0,4	9,505E-111	7,7199E-85	1,8063E-74	1,4484E-71	1,8063E-74	7,7199E-85		

# aff	150									
# non aff	850									
pAi non aff		0	0,1	0,2	0,3	0,4	0,5			
Δ pAi	0,05	2,1561E-20	0,00994614	0,04896055	0,08358651	0,10417953	0,11025423			
Δ pAi	0,1	2,0126E-39	5,571E-07	0,00010149	0,00058665	0,00119145	0,00139743			
Δ pAi	0,15	1,1091E-58	2,7555E-13	8,462E-09	2,9851E-07	1,2395E-06	1,6229E-06			
Δ pAi	0,2	3,2726E-78	2,1683E-21	3,2211E-14	1,1049E-11	1,111E-10	1,5638E-10			
Δ pAi	0,25	4,9576E-98	4,4952E-31	6,5226E-21	3,1015E-17	2,5169E-16	1,1763E-15			
Δ pAi	0,3	3,749E-118	3,6987E-42	8,129E-29	6,9335E-24	5,4331E-22	6,5657E-22			
Δ pAi	0,35	1,383E-138	1,6797E-54	7,1058E-38	1,2938E-31	2,9415E-29	2,5869E-29			
Δ pAi	0,4	2,435E-159	5,4915E-68	4,8846E-48	2,1003E-40	1,3332E-37	6,8178E-38			

aff affected individuals
 # non aff non affected individuals
 pAi non aff allele frequency in non affected individuals
 Δ pAi % Difference in allele frequency between affected and non-affected individuals

Figure 3 (II)

6/16

p-VALUE DISTRIBUTION

# aff	# non aff	pAi	non aff	0	0,1	0,2	0,3	0,4	0,5
Δ pAi		0,05	1,0628E-12	0,00789803	0,03942584	0,06867566	0,08621572	0,09083704	
Δ pAi		0,1	3,4525E-24	4,4217E-07	5,6883E-05	0,00031976	0,0006363	0,00070881	
Δ pAi		0,15	5,9036E-36	4,3025E-13	3,3635E-09	9,2134E-08	3,319E-07	3,5871E-07	
Δ pAi		0,2	4,7325E-48	1,5566E-20	1,0346E-14	1,7218E-12	1,1512E-11	1,00471E-11	
Δ pAi		0,25	1,6694E-60	3,5436E-29	2,0473E-21	2,2178E-18	1,1498E-17	1,3524E-17	
Δ pAi		0,3	2,4613E-73	7,2498E-39	3,0748E-29	2,0601E-25	3,4525E-24	7,4807E-25	
Δ pAi		0,35	1,4447E-86	1,6945E-49	3,9559E-38	1,4118E-33	2,662E-32	1,4118E-33	
Δ pAi		0,4	3,214E-100	5,3051E-61	4,7325E-48	7,1282E-43	1,0691E-41	7,2652E-44	

# aff	# non aff	pAi	non aff	0	0,1	0,2	0,3	0,4	0,5
Δ pAi		0,05	6,4766E-24	5,7827E-05	0,00172627	0,00551541	0,00882876	0,00978249	
Δ pAi		0,1	6,5309E-47	3,065E-14	1,0301E-09	4,3205E-08	1,8833E-07	2,2731E-07	
Δ pAi		0,15	1,1969E-70	2,0716E-27	3,7441E-19	4,6626E-16	6,9719E-15	6,9719E-15	
Δ pAi		0,2	3,3252E-95	1,1636E-43	1,6614E-31	8,5632E-27	4,1421E-25	1,9885E-25	
Δ pAi		0,25	1,227E-120	1,7683E-62	1,5329E-46	3,1722E-40	8,6765E-39	3,6071E-39	
Δ pAi		0,3	5,303E-147	1,526E-83	4,2697E-64	2,5968E-56	3,9328E-54	2,5968E-56	
Δ pAi		0,35	2,36E-174	1,184E-106	4,5658E-84	4,7426E-75	4,26245E-73	4,0958E-77	
Δ pAi		0,4	9,446E-203	1,082E-131	2,137E-106	1,8014E-96	3,3252E-95	6,725E-102	

aff affected individuals
 # non aff non affected individuals
 pAi non aff allele frequency in non affected individuals
 Δ pAi % Difference in allele frequency between affected and non-affected individuals

Figure 3 (III)

7/16

004710 54069460

ALLELIC ASSOCIATION
3,000 MARKERS MAP

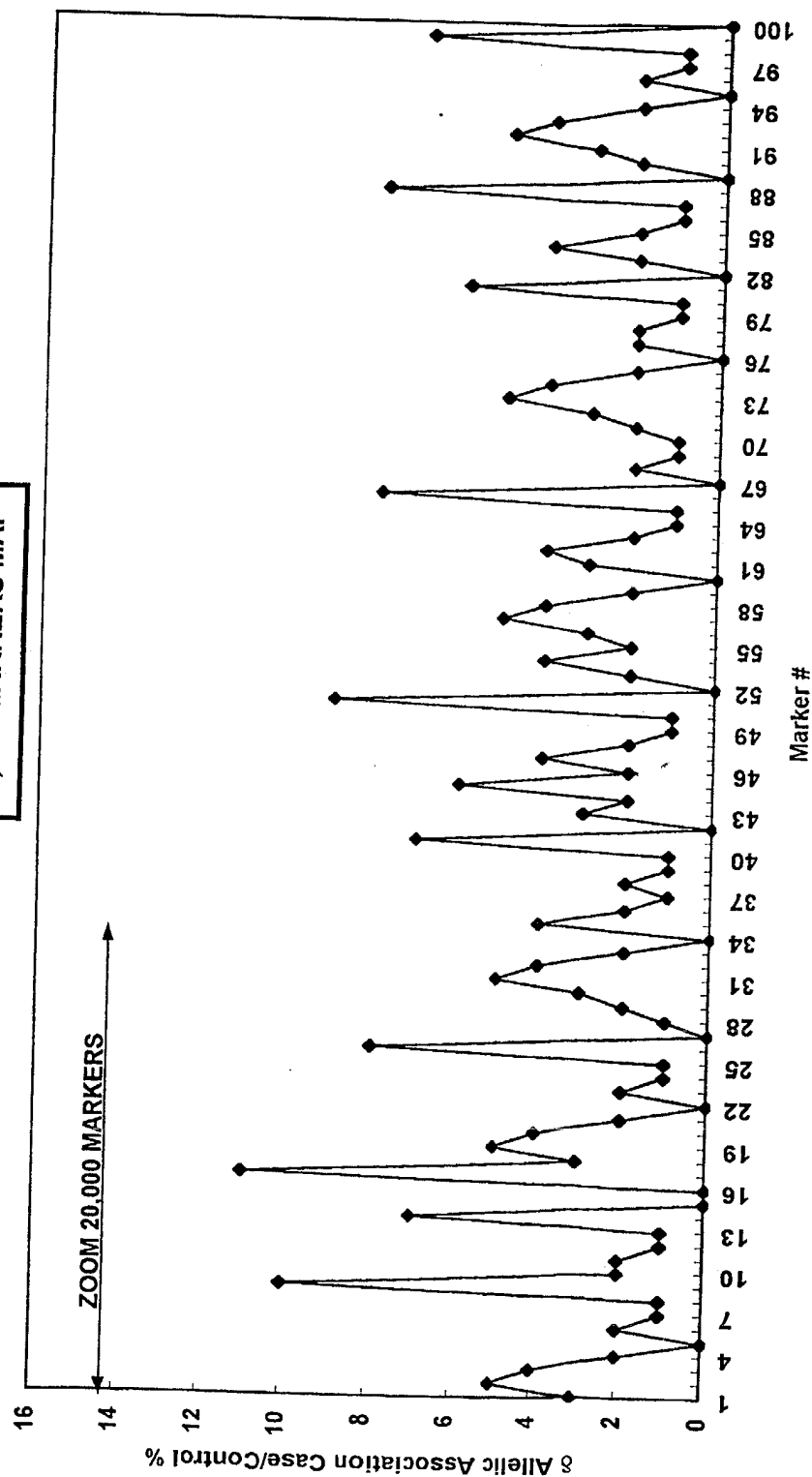


Figure 4

004770" 520E9460

WO 99/04038

09/463075
PCT/IB98/01193

8/16

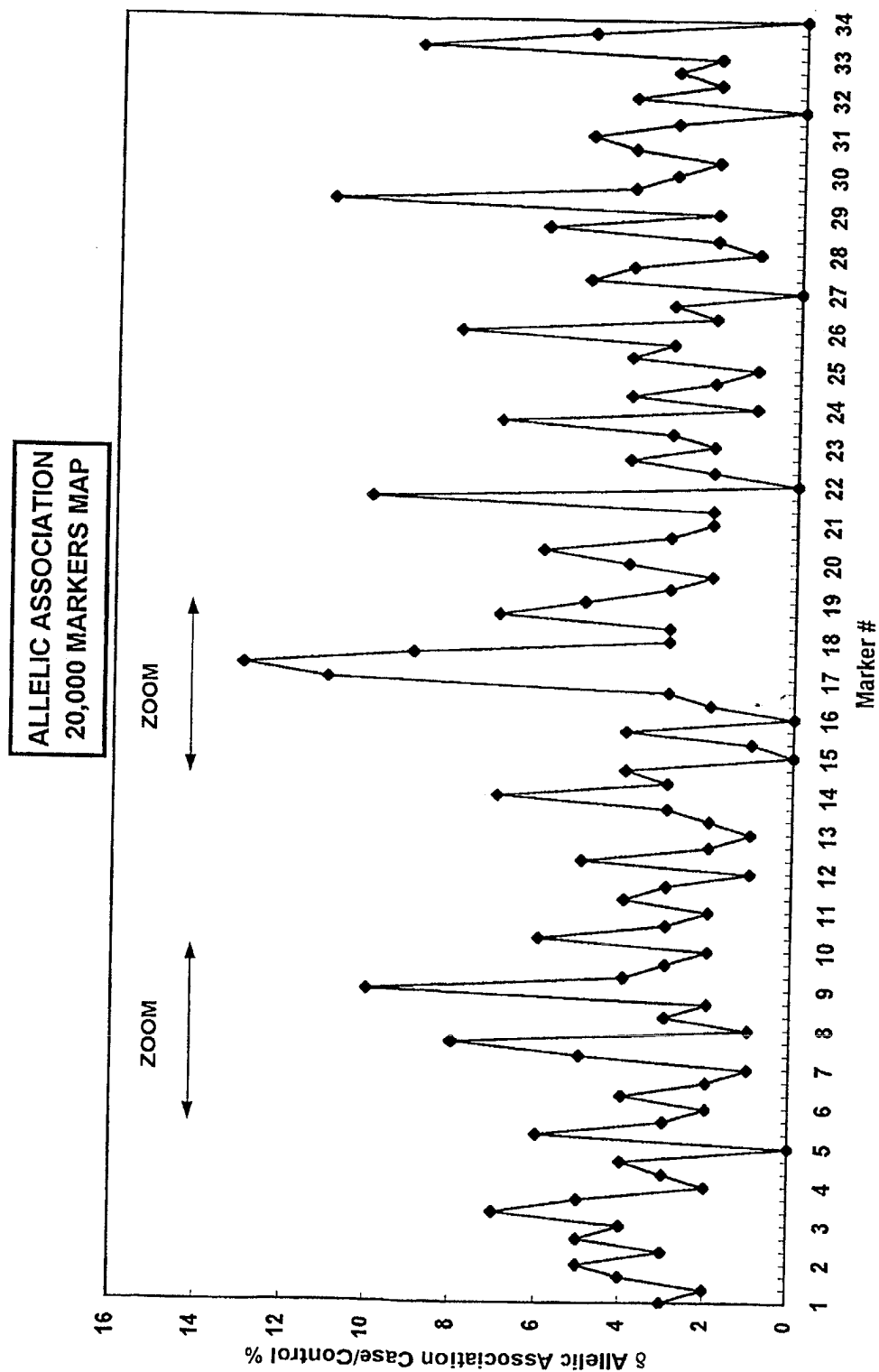


Figure 5

9/16

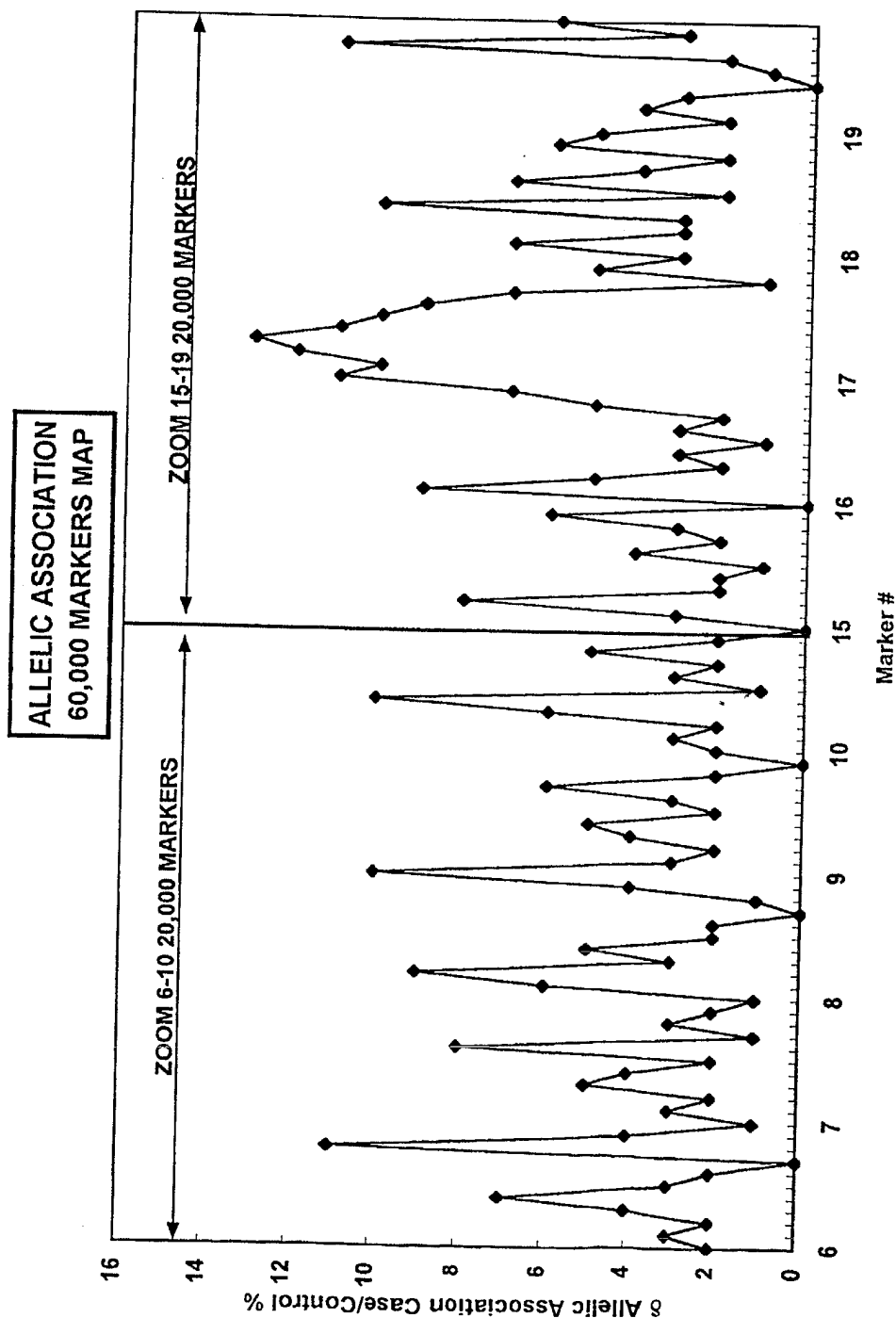


Figure 6

APO E REGION HAPLOTYPE FREQUENCY ANALYSIS

POPULATIONS	AD CASES (225)	AD CONTROLS (248)
-------------	----------------	-------------------

markers	99-366	99-344	99-359	99-355	haplotype frequencies		odds-ratio	P value
p value	3,01E-01	1,11E-01	6,63E-01	1,38E-01	cases	controls		
haplotype 1	C	G			0,404	0,308	1,52	3,05E-03 ***
haplotype 2		G	A		0,203	0,165	1,29	1,24E-01 *
haplotype 3			G	G	0,375	0,306	1,36	2,83E-02 **
haplotype 4	C		A		0,264	0,209	1,36	5,95E-02 **
haplotype 5		G		A	0,115	0,071	1,70	1,64E-02 **
haplotype 6	C			A	0,15	0,129	1,19	3,59E-01 *
haplotype 7	T		G	G	0,225	0,122	2,09	4,76E-05 *****
haplotype 8	T	A	G	G	0,228	0,108	2,44	2,05E-06 *****

Figure 7

004440" 520E9460

APO E REGION HAPLOTYPE SIMULATION
POPULATION : 225 CASES vs 248 CONTROLS

WO 99/04038

11/16

09/463075
PCT/IB98/01193

Haplotype 8	4 Markers				haplotype frequencies		odds- ratio	pvalue
	99-344/439	99-366/274	99-359/308	99-355/219	cases	controls		
A		T	G	G	0,228	0,108	2,44	2,05E-06 *****

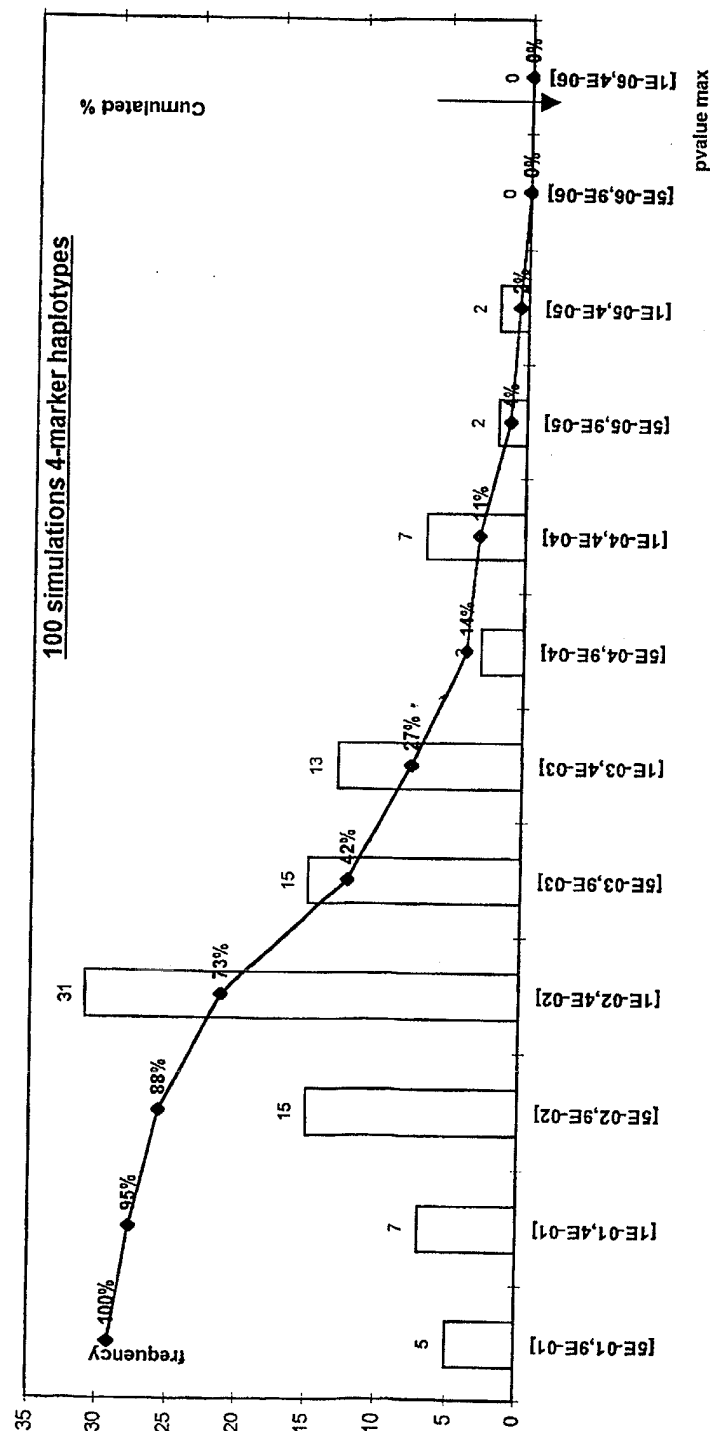


Figure 8

09463075 .01400

WO 99/04038

09/463075
PCT/IB98/01193

12/16

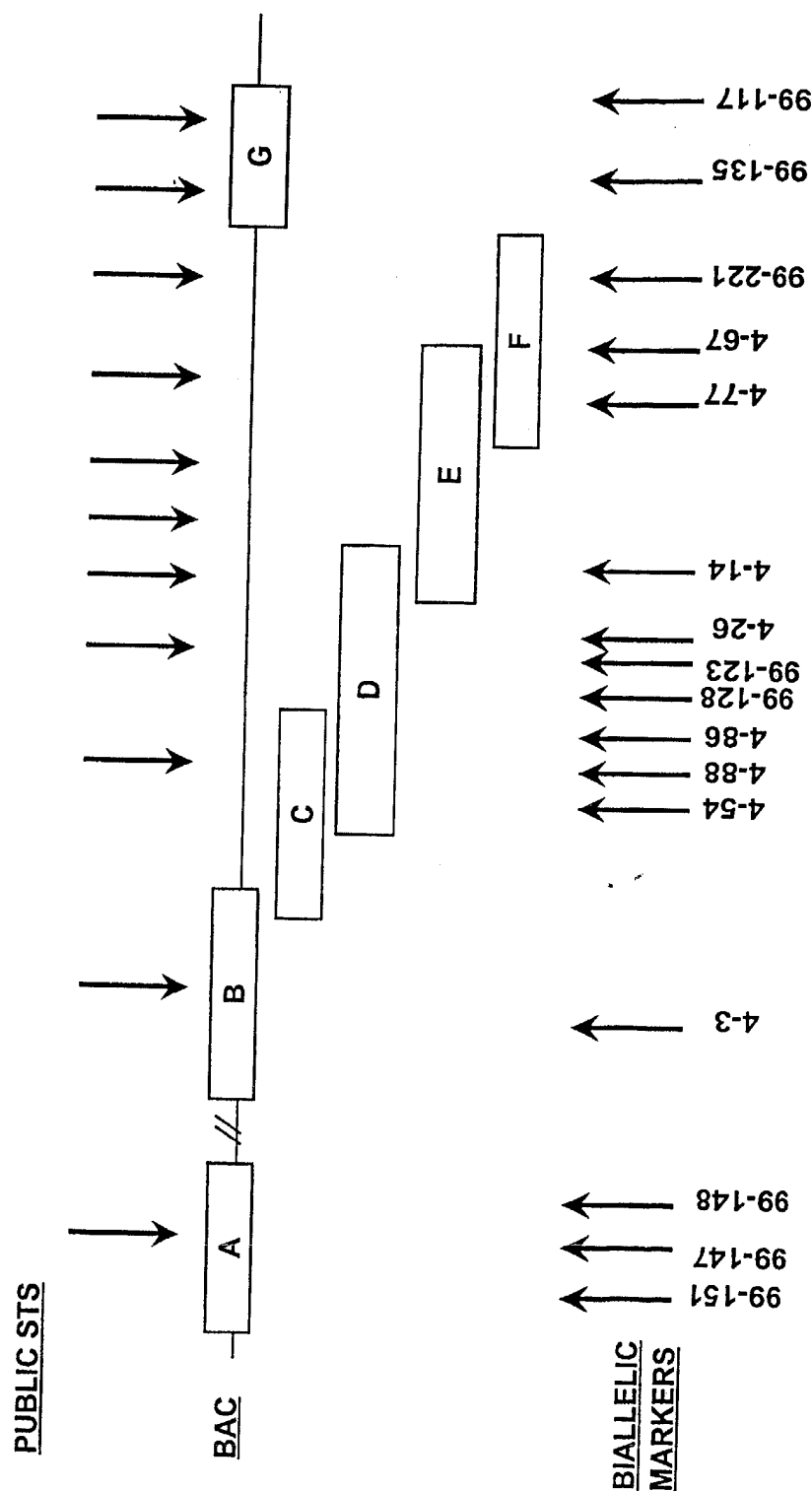


Figure 9

PROSTATE CANCER ASSOCIATION STUDIES (FIRST SCREENING)

Population Sample size	PROSTATE CANCER CASES = 112	NON AFFECTED CONTROLS=76
Population Characteristics	35 sporadic cases + 77 familial cases	> 65 years PSA<4

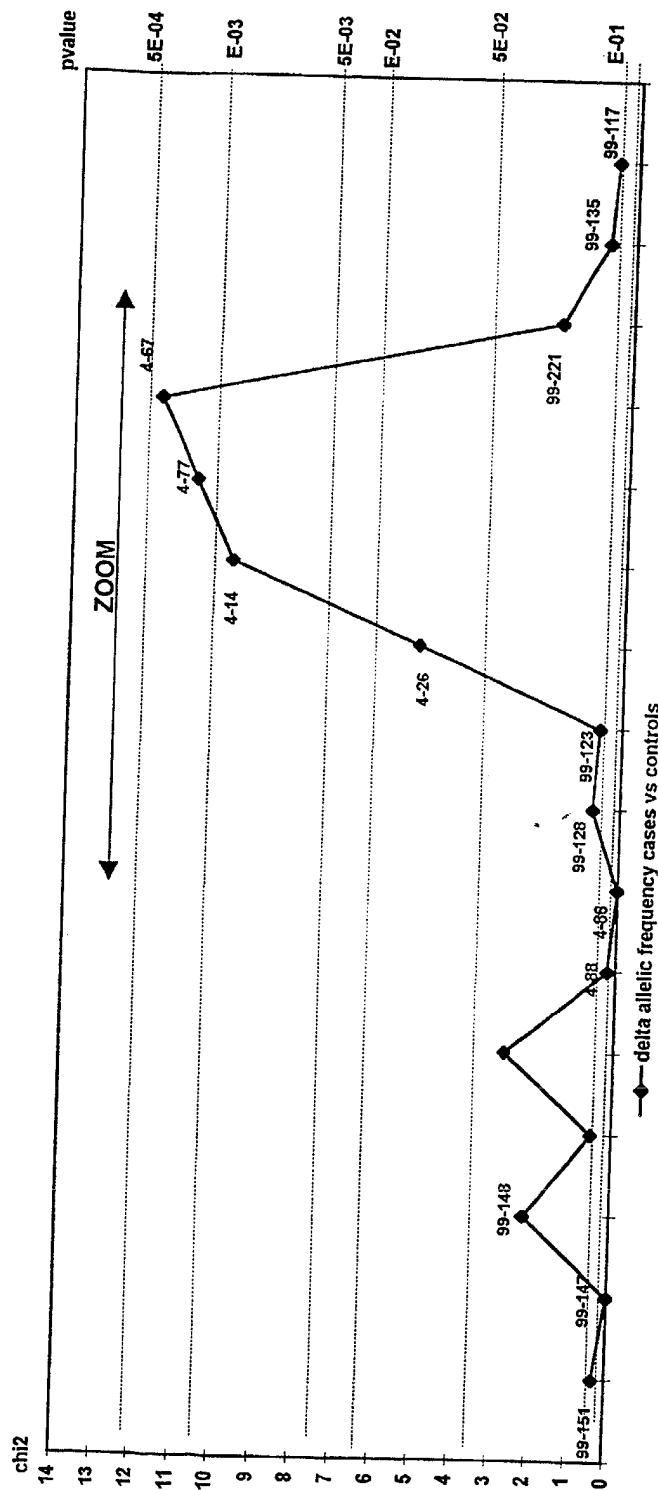


Figure 10

PROSTATE CANCER ASSOCIATION STUDIES (ZOOM)

	PROSTATE CANCER CASES (185)	NON-AFFECTED CONTROLS (104)
characteristics of populations	47 sporadic cases + 138 familial cases	> 65 years PSA<4

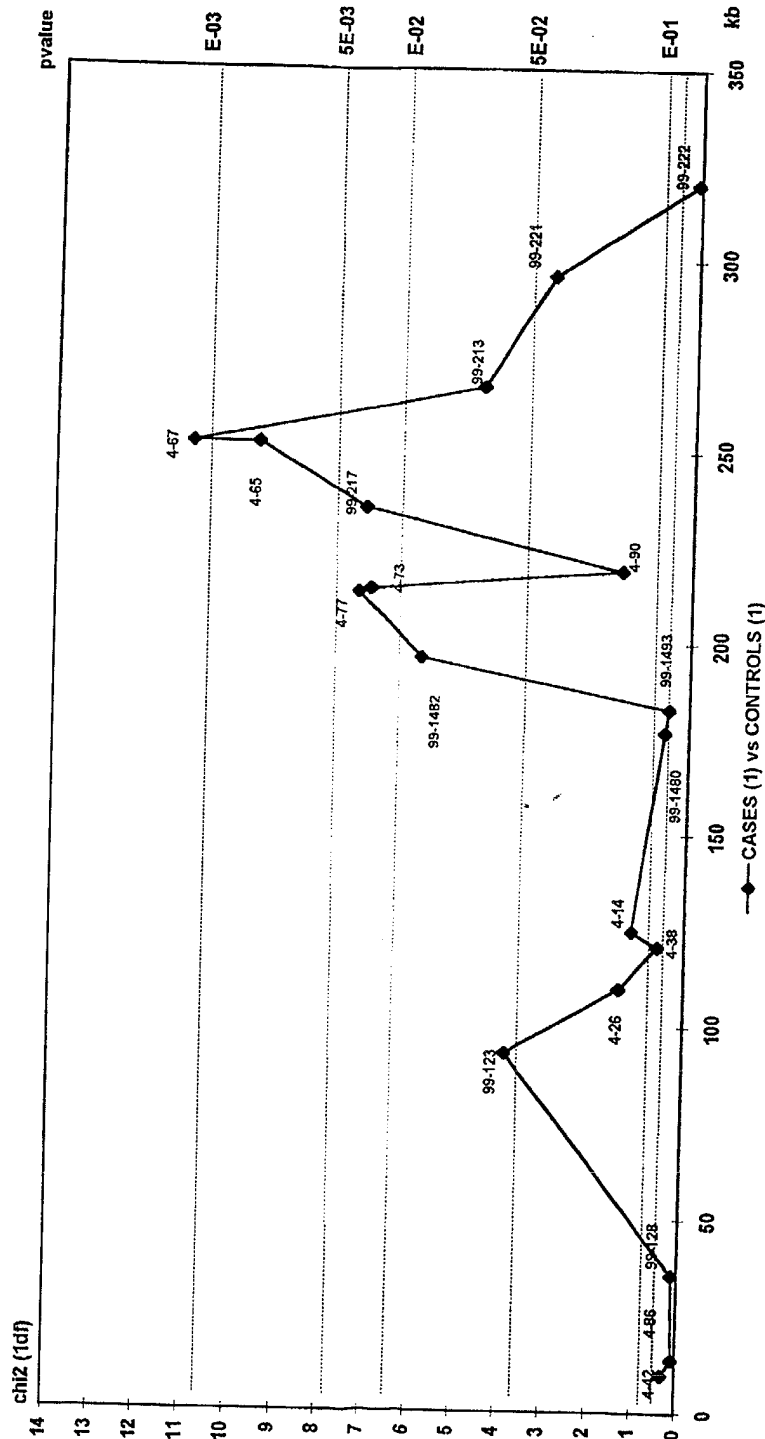


Figure 11

PROSTATE CANCER HAPLOTYPE FREQUENCY ANALYSIS

	PROSTATE CANCER	NON-AFFECTED
	CASES (281)	CONTROLS (130)
characteristics of populations	143 sporadic cases + 138 familial cases	> 65 years PSA<4

markers	99-123	4-26	4-14	4-77	99-217	4-67	99-213	99-221	99-135	haplotype frequencies	relative risk	pvalue
BACs	C	E	E	F	F	F	F	F	G			
genes	PG1									cases	controls	pvalue
p value	2,00E-01	1,00E-01	1,00E-01	2,00E-02	2,00E-02	6,00E-04	9,00E-02	7,00E-01	2,00E-01			
haplotype 8 >304kb<	C	A	C	G	T	T	C	A	A	0,075	0,018	9,00E-04 ***
haplotype 7 >286kb<		A	C	G	T	T	C	A	A	0,095	0,016	6,00E-05 ****
haplotype 6 <186kb>		A	C	G	T	T	C	A		0,116	0,019	1,00E-05 *****
haplotype 5 <171kb>			C	G	T	T	C	A		0,117	0,013	9,00E-07 *****
haplotype 4 <83kb>				G	T	T	C	A		0,117	0,025	2,00E-05 *****
haplotype 3.1 <54kb>					T	T	C	A		0,117	0,027	2,00E-05 *****
haplotype 3.2 <54kb>				G	T	T	C			0,222	0,109	4,00E-05 *****
haplotype 2.2 <39kb>				G	T	T				0,251	0,134	2,00E-04 ****
haplotype 2 <32kb>					T	T	C			0,226	0,112	1,00E-04 ****
haplotype 1.1 <17 kb>					T	T				0,256	0,146	3,00E-04 ****
haplotype 1.2 <15 kb>						T	C			0,233	0,129	6,00E-04 ****

Figure 12

16/16

PROSTATE CANCER HAPLOTYPE SIMULATIONS (100 ITERATIONS)

markers	4-14	4-77	99-217	4-67	99-213	99-221	haplotype frequencies		relative risk	pvalue
							cases	controls		
haplotype	C	G	T	T	G	A	0,117	0,013	10,06	9,00E-07

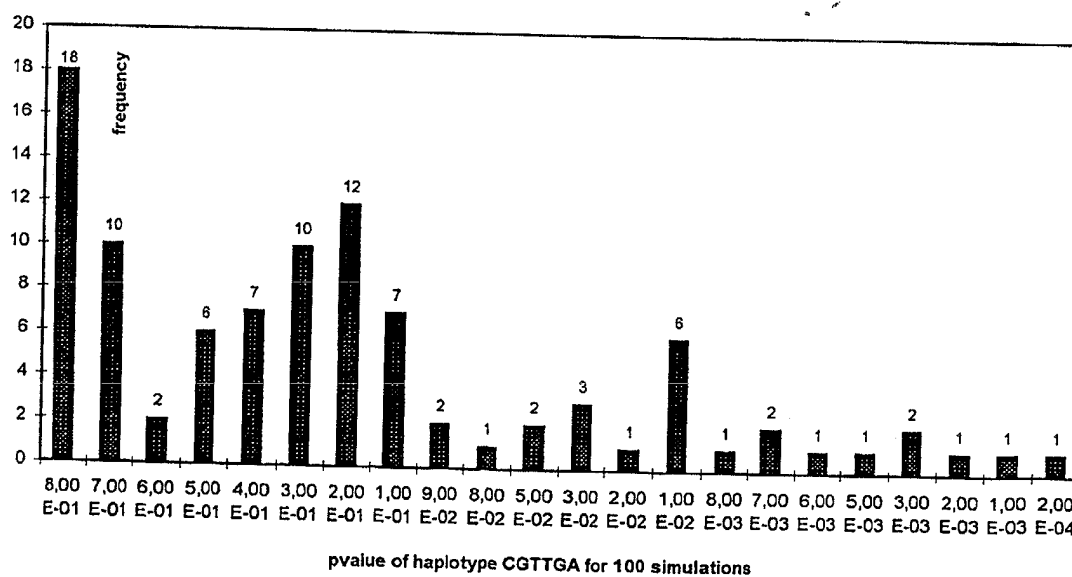
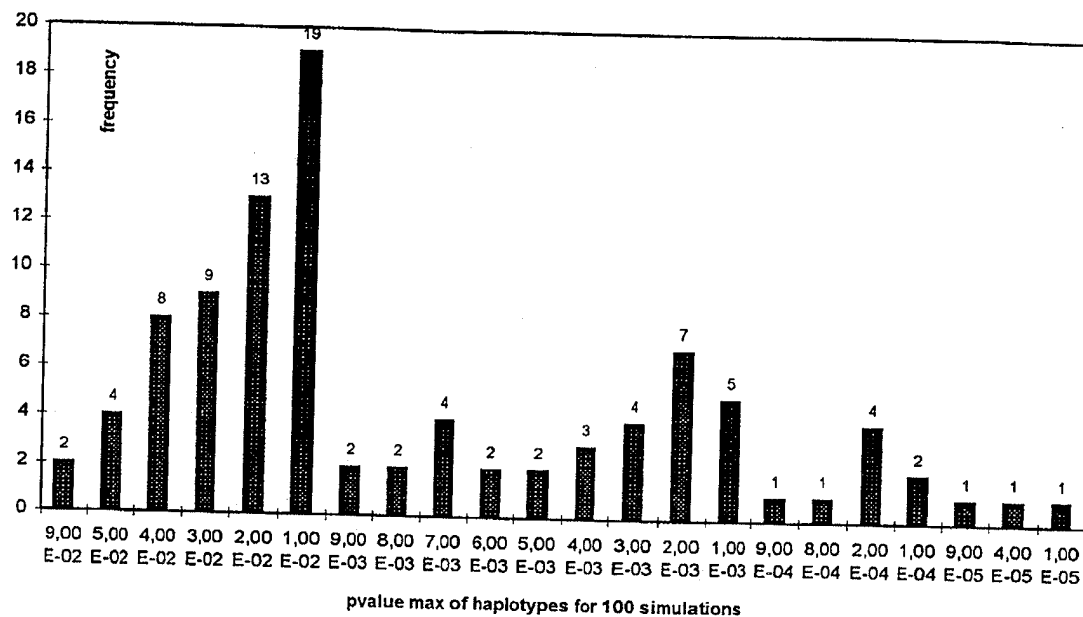


Figure 13